.DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN RENAL MASSES

Dissertation submitted to

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M.CH (UROLOGY) –BRANCH -IV

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DECLARATION

I solemnly declare that this dissertation entitled, **"DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN RENAL MASSES"** is a bonafide work done by me in Department of Urology, Madras Medical College and Government General Hospital , under the guidance and supervision of the Professor **R.Jeyaraman, M.S,M.Ch(Uro).,** Professor and Head of Department, Department of Urology, Rajiv Gandhi Government General Hospital,Chennai.This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, in partial fulfillment of requirement for the award of Degree of **M.Ch Urology.**

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CERTIFICATE

This is to certify that the dissertation title **" DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN RENAL MASSES "** submitted by DR.D.MOHANKUMAR appearing for M.Ch(Urology) degree examination in August 2014 is a bonafide work done by him under my guidance and supervision in fulfilment of requirement of the Tamilnadu Dr. M.G.R. Medical University. I forward this to The Tamilnadu Dr. M.G.R. Medical University,Chennai.

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INDEX

SL .NO	CONTENTS	PAGE NO
1	Introduction	1
2	Aim And Objectives	3
3	Review Of Literature	4
4	Materials And Methods	35
5	Observation And Results	39
6	Discussion	47
7	Conclusion	53
8	Bibliography	54
9	Appendix	59
	Appendix 1 : Consent Form	
	Appendix 2 :Proforma	
	Appendix 3 :Master Chart	
	Appendix 4 :Ethical Committee Approval	
	Appendix 5:Plagiarism	

INTRODUCTION

Renal cell carcinoma is a common urological cancer. Patients usually presents with loin pain and haematuria. CT and MRI are the two important investigations that are available to diagnose and stage renal masses. The density of a renal mass and its intensity on unenhanced imaging and the presence of enhancement after contrast administration has been used to determine the nature of renal masses.

In case of a cystic renal mass, the Bosniak classification uses the CT or MR imaging appearances and it stratifies the risk of malignancy associated with the renal cyst. In the recent times ,contrast CT has been used to differentiate clear cell renal cancer from papillary renal cell cancer in which the later usually has a homogenous appearance whereas the former has a heterodense appearance .

Inspite of these investigations there are no imaging techniques that easily differentiate the benign renal mass from the malignant which is shown by the fact that about 20% of nephrectomies are done on benign lesions .Therefore, preoperative imaging studies would play an important diagnostic role if they could be used to precisely differentiate between the two categories of renal masses .

Diffusion weighted MRI is being used in neuroradiology for the diagnosis of differentiation between the benign and malignant tissue. The diffusion of molecules within the cell follows Brownian movement. The highly cellular malignant tissue has restricted diffusion and the benign lesions have a high diffusion coefficient. The restricted diffusion images have a low ADC value and the benign lesions have high ADC value.

AIM OF THE STUDY

To predict the histopathological nature of renal masses by using Diffusion weighted Magnetic Resonance Imaging (DW MRI)

To study the correlation of DW MRI findings with clinical, radiological and pathological findings.

REVIEW OF LITERATURE

Kidneys are retroperitoneal organs located in the dorsal aspect of the abdomen on each side of the vertebra. The upper pole of each kidney lies opposite the T 12 vertebra, and the lower pole lies opposite to the L3 vertebra. The right kidney is usually more caudal in position. The weight of each kidney measures 125 g to 170 g in the male and from 115 g to 155 g in the female. The human kidney is about 11 cm to 12 cm in length, 5.0 cm to 7.5 cm in width, and 2.5 cm to 3.0 cm in antero posterior diameter . On the medial surface of each kidney is the hilus, through which the renal pelvis, the renal artery and vein, the lymphatics, and a nerve plexus pass into the sinus of the kidney.

The renal artery enters the hilar region and it divides to form an anterior and a posterior branch. The anterior branch divides into three segmental arteries and supply the upper, middle, and lower thirds of the anterior surface of the kidney . The posterior branch of renal artery supplies the posterior surface and occasionally gives rise to a small apical segmental branch. There are no collateral circulation between the segmental or lobar arteries or their subdivisions.

The kidney has two distinct regions , a pale outer region, the cortex, and a darker inner region, the medulla . The medulla has 8 to 18 striated conical masses called the renal pyramids. The base of the pyramid is located at the

corticomedullary junction , and the apex is toward the renal pelvis and it forms the papilla. On the tip of each papilla there are 15 to 20 small openings .They are the distal ends of the collecting ducts .

The medulla is divided into an inner and an outer zone, with the outer zone subdivided into an inner and an outer stripe . The inner medulla contains both descending and ascending thin limbs of loop of henle and large collecting ducts, including the ducts of Bellini. In the inner stripe of the outer medulla, thick ascending limbs are present in addition to descending thin limbs and collecting ducts. The outer stripe of the outer medulla contains the terminal segments of the pars recta of the proximal tubule, the thick ascending limbs (partes rectae of the distal tubule), and collecting ducts. The division of the kidney into cortical and medullary zones and the further subdivision of the medulla into inner and outer zones is of great importance in relating kidney to the ability to form a maximally concentrated urine.

BENIGN RENAL LESIONS

Renal cysts

Renal cysts are the most common benign lesions of the kidney. They account for more than 65% of renal masses. They are usually asymptomatic. They can be either solitary, multiple and bilateral. The Bosniak classification for renal

cysts, is the most often used method for characterizing renal cysts and for determining the likelihood of the presence of associated malignancy within the cyst. There is an increased risk of malignancy in Bosniak class III and IV and hence therapy is recommended**.**

ANGIOMYOLIPOMA

Angiomyolipoma constitutes about 8% of the renal tumors. It is a benign tumor that consists of vessels, smooth muscle,mature adipose tissue. It may be either sporadic or familial.The usual mode of a sporadic presentation is of a middle-aged female with a single asymptomatic tumor. Usually they grow slow and are detected incidentally. It is the most common renal mass lesion that is associated with spontaneous perirenal hemorrhage, the next being RCC.AML is usually associated with tuberous sclerosis in 20 to 30 percent of patients. The presence of fat −20 Hounsfield Units is considered diagnostic of AML. The differential diagnosis include liposarcoma, fat containing RCC, and fat poor angiomyolipoma resembling an RCC. The treatment of AML depends on the size, symptoms and patient factors. Lesions less than 4 cm are usually managed conservatively with repeat scan at 6 to 12 months. Surgery should be reserved for those symptomatic , age, comorbid conditions and in women of childbearing age . In tuberous sclerosis or in multiple tumors nephron sparing surgery should be done.

CYSTIC NEPHROMA

Cystic nephroma has bimodal age distribution and usually it occurs in first 2 to 3 years of life, males, and also in fifth decade. The male to female ratio is 1:8. The symptoms are abdominal mass, pain, and hematuria, but cystic nephromas are usually diagnosed incidentally.They are solitary, centrally located, showing curvilinear calcifications, and herniation into the pelvi calyceal system, and septal enhancement .So the radiologic differentiation between cystic nephroma

and cystic RCC is difficult. They are well encapsulated, and has a fibrous pseudocapsule. It has cysts lined by flattened, cuboidal epithelium.IHC shows positive for CD10,calretinin, inhibin, estrogen, and progesterone receptors .In children where there is a doubt in the diagnosis of wilms tumor, nephrectomy is done.

ONCOCYTOMA

This benign renal tumor is clinically and radiographically indistinguishable from RCC. There is a higher incidence of oncocytoma in elderly patients with a small renal mass as compared to younger patients. They originate from the distal tubules, which is similar to chromophobe RCC. This may represent as a spectrum of disease as evidenced in Birt-Hogg-Dubé genetic syndrome, but there is no study that states that oncocytomas transform into malignant transformation in sporadic

cases. If oncocytoma is suspected , a percutaneous core biopsy may reliably provide a diagnosis. Frozen section during surgery does not distinguish the oncocytoma from RCC and this should not be done to plan the treatment strategy.

METANEPHRIC ADENOMA

Metanephric adenoma is a recently described, rare benign mass that is not differentiated from RCC radiologically. It is usually found incidentally, and predominantly occurs in females. It occurs in the fifth decade . The diagnosis is done after surgical excision and can be confirmed with IHC for cytokeratins,WT1, S-100, and AMACR.

RISK FACTORS - RCC

RCCs arises from the proximal convoluted tubules and the most common histologic subtypes that arise from them are clear cell ca and papillary RCC. But the newer studies states that the chromophobe and collecting duct RCC, the other less common types, are usually derived from the more distal components of the nephron .

The most important risk factor for Renal Cell Carcinoma is tobacco exposure. The relative risk of RCC with the use of tobacco has been modest which ranges from 1.4 to 2.5 when compared with that of controls. The risk of RCC has been implicated with the use of tobacco of all forms and the risk increases with

increasing dose of tobacco or pack-years .Relative risk of RCC is directly proportional to the duration of smoking and the number of smokes per day and the risk begins to fall after stopping tobacco use, further supporting a cause and effect relationship .

The next major risk factor for RCC is Obesity. For each unit of increasing body mass index , there is an increase in the relative risk by 1.07. In Western countries where there is increased prevalence of obesity there is an increased incidence of RCC .Recent estimates from the united states shows that about one third of the RCC has an increased body mass index. Potential mechanisms that links obesity to RCC are numerous. Lipid peroxidation leading to the damages in DNA , increased expression of insulin-like growth factor-1, increased circulating levels of estrogen, and increased arteriosclerosis in the renal tissue and local inflammation are the mechanisms for the development of RCC in obesity.

Hypertension is an important factor for the development of RCC. Diuretics are also thought of as a significant risk factor in RCC but further evidence suggests that the drug is not the factor and the disease is the cause. The proposed mechanisms for the development of RCC are that Hypertension produces renal injury and it also causes inflammation associated with metabolic or functional changes in the nephron tubules that may increase susceptibility to carcinogens .

Viruses , lead compounds and benzene compounds are risk factors in others where there are no studies that say that these above mentioned factors are a risk factor for RCC. Chloroform exposure as once thought in the risk factor group was not so as there are many bias in the studies conducted.But the VHL gene is mutated when there is a chloroform exposure.Workers from asbestos or cadmium industries are at relatively increased risk of RCC.

There are many Case control studies that has shown that Renal cell carcinoma is more common in poor economic status and city population but the relationship for the risk of RCC has not been told in the study. The Western diet which typically includes a high fat,high protein, and low fruits and vegetables, or when there is increased intake of dairy products, and increased consumption of coffee or tea have been associated with increased risk of RCC, but the relative risk is only modest, and the data is conflicting in most instances . A family history of RCC is also a risk factor for RCC. One study reports a relative risk of 2.9 for persons with a first- or second-degree relative with RCC .

Thorotrast (a contrast agent), and radiation therapy for malignancy is also a risk factor for RCC.The relative risks are low for the above reported causes.But only few cases of RCC developed in post testicular ca radiation therapy or post wilms tumor radiation therapy. There is an increased incidence of RCC that is also

seen in patients with chronic kidney disease and in patients with tuberous sclerosis.

PATHOGENESIS

Renal cell carcinoma arises from the proximal convoluted tubule and it comprises of 90% of the kidney tumour in adults. RCC has diverse clinical, pathological, and molecular characteristics and hence there are distinct prognosis and therapeutic responses between those groups.

PATHOLOGICAL CLASSIFICATION OF RCC

The pathological classification of RCC is providing relevant prognostic information and guidance to therapy. As the development of molecular mechanisms of renal tumors has been strongly elucidated, molecular classification is to be eventually replaced by morphological classification in the near future.

Histologic Subtypes of Renal Cell Carcinoma

CLEAR CELL RCC

Clinical Features

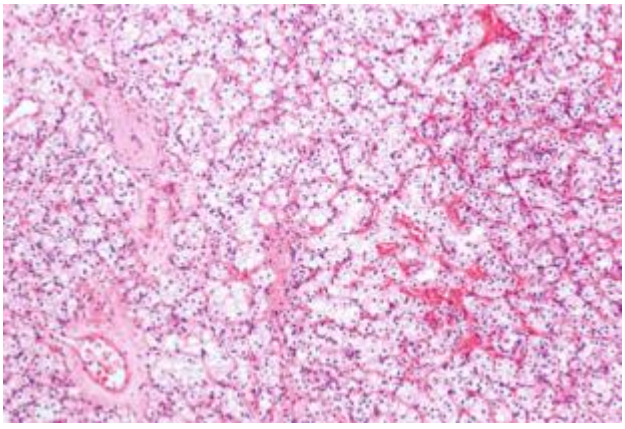
Clear cell RCC is the most common subtype and it accounts for 70% of all RCCs. It is most common in the sixth to Seventh decade. The males to

female ratio is approximately 2:1 .Clear cell RCC is usually sporadic and only 2-4% are familial.

Familial cases occur at a younger age and they are most likely to be multifocal and bilateral.

Pathology

Clear cell RCC is usually unilateral and unicentric. It is round and appears as a exophytic mass with a fibrous capsule. It has a golden yellow colour and variegated appearance with different degrees of hemorrhage, necrosis,and calcification[6] . Microscopically the tumor cells are arranged in sheets,alveolar, or acinar structures . They have clear cytoplasm due to tissue processing and the loss of glycogen and lipid.



Clear cell RCC

Molecular Genetics

Clear Cell RCCs has chromosome 3p mutations which includes deletion, mutation, or methylation in the von Hippel–Lindau (VHL) gene on chromosome 3p25-26.

Somatic mutations in VHL gene has been found in 18–82% of sporadic RCC

The heterozygosity loss in the VHL locus is seen in 98% of cases. Hypermethylation of the VHLgene is seen in 5–20% of patients. Others show

allelic loss or LOH at the VHL locus, which is the Knudson's two-hit model of malignant transformation.The VHL regulates the Hypoxia-inducible factor (HIF) . Consequently, HIF levels stimulates VEGF, PDGF, TGF- a , CA IX.Also the PI3 kinase ,mTOR pathway and Ras-raf pathway are activated which are involved in cell proliferation and survival. These pathways produce angiogenesis and prevent apoptosis and better survival of cells under hypoxic conditions.

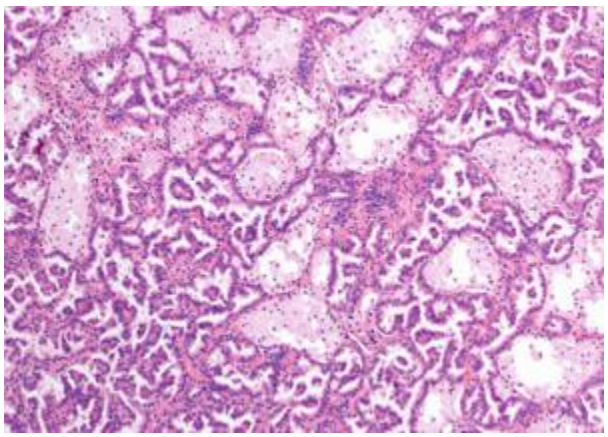
PAPILLARY RCC

CLINICAL FEATURES

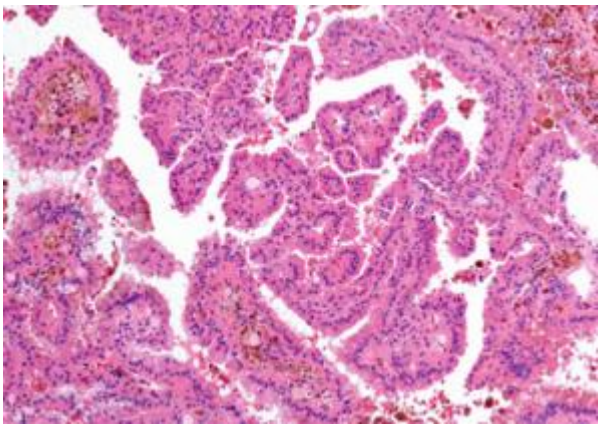
Papillary RCC is the next most common type of RCC and it comprises of 10–15% of RCCs. Papillary RCC is a better prognostic tumor. Most of them occur sporadically, but hereditary Papillary RCC are also seen.

Pathology

Papillary RCC presents as a well circumscribed mass which has a pseudocapsule[7]. Few tumors are necrotic and friable. Papillary RCC are usually bilateral and multifocal . Microscopically, Papillary RCC has different proportions of papillae, tubulopapillae, and tubules. The papillae has fibrovascular cores with foamy histiocytes.Two subtypes of Papillary RCC are present depending upon the histology. The Type I tumor which accounts for two thirds of cases contains short papillae with single layer of cells, scant cytoplasm and low-grade nuclei . On the other hand the Type II tumor has large papillae and cells with abundant eosinophilic cytoplasm,large pseudostratified nuclei and prominent nucleoli .Type II tumors have poor prognosis when compared to the former.



TYPE I PAPILLARY RCC



TYPE II PAPILLARY RCC

Molecular Genetics

Trisomy 7, 17, and loss of Y chromosome is the most common finding in Papilllary RCC. Gain of 7p and 17p is seen in type I tumors . 9p deletion is present in 20% of PRCC and loss of heterozygosity at 9p13is present in type II tumors.

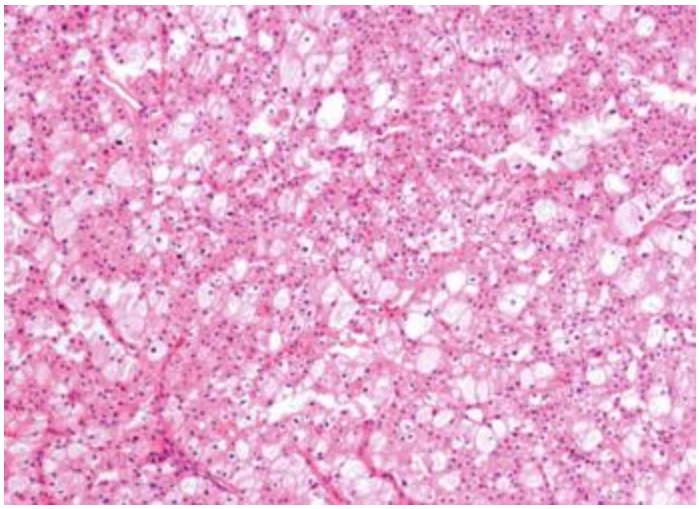
CHROMOPHOBE RCC

CLINICAL FEATURES

Chromophobe RCC constitutes 5% of RCCs and it arises from the intercalated cells of the collecting ducts . Chromophobe RCC age range is in the fifth decade. Males and females are affected equally. It has better prognosis than Clear Cell RCC.

Pathology

Chromophobe RCC appears as a solitary, well-circumscribed mass that is nonencapsulated and it is homogenous ,light brown in colour on cut surface[8]. Hemorrhage, necrosis is uncommon.Microscopically, the cells are arranged in solid sheets,which are large and polygonal . They have fine reticulated cytoplasm which is due to cytoplasmic microvesicles.



CHROMOPHOBE RCC

The nuclei are hyperchromatic and irregular with perinuclear halos , which has a plant cell like appearance. The tumor has intensely eosinophilic cytoplasm, termed eosinophilic variant .

Molecular Genetics

Chromophobe RCC has loss of chromosome Y, 1, 2,6, 10,13, 17, and 21 . It can occur in BHD syndrome, with mutations in Birt Hogg Dube gene (BHD) 17p11.2, which encodes the protein folliculin .But sporadic chromophobe RCC has rare mutations in the BHD gene.

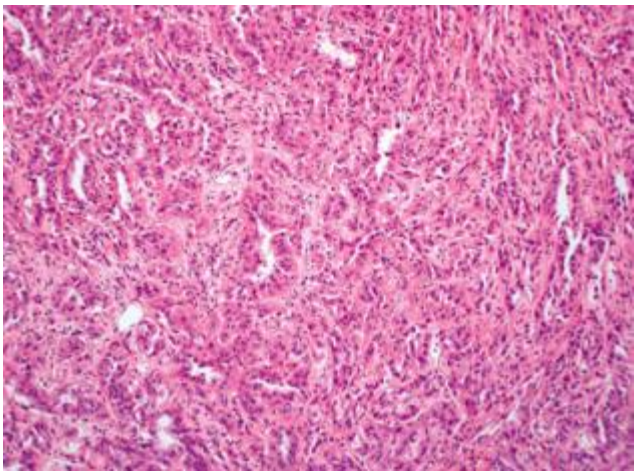
RENAL CELL CARCINOMA, UNCLASSIFIED TYPE

Unclassified type, is the term used when the histological type does not fit into any of the decribed histological varieties. This is a not a true biological entity

but a diagnostic category. These are a heterogeneous group of malignancies with poorly defined clinical, morphological, or genetic features. RCC subtypes with sarcomatoid morphology without recognizable epithelial elements, mucin production, mixtures of epithelial and stromal elements and unrecognizable cell types are included.These tumors are poorly differentiated and have a poor prognosis.In published series the assignment to this category varies from 0.7% to 5.7%

COLLECTING DUCT CARCINOMA

This is a rare subtype of RCC which constitutes 0.4 to 1.8 % of RCC. These tumors are highly aggressive and presents at an advanced age with poor prognosis. This occurs at a wide patient age range with male predominance of 2:1 .These are large with firm white to gray appearance with irregular borders and areas of necrosis. Histology shows a infiltrative tubular or tubulopapillary pattern. It has dense desmoplastic reaction with higher nuclear grade. The molecular pathway is poorly understood. Monosomy of chromosome 1,6,4,15 and 22 with allelic loss of chromosomal arms 1q ,6p,8p 13q and 21q are reported. Two thirds of collecting duct RCC has a minimal deletion in 1q 32.1 region.



COLLECTING DUCT CARCINOMA

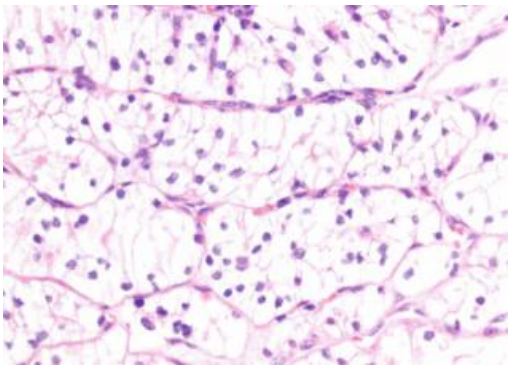
PATHOLOGICAL PROGNOSITIC PARAMETERS FOR RENAL CELL CARCINOMA

Fuhrman Nuclear Grading

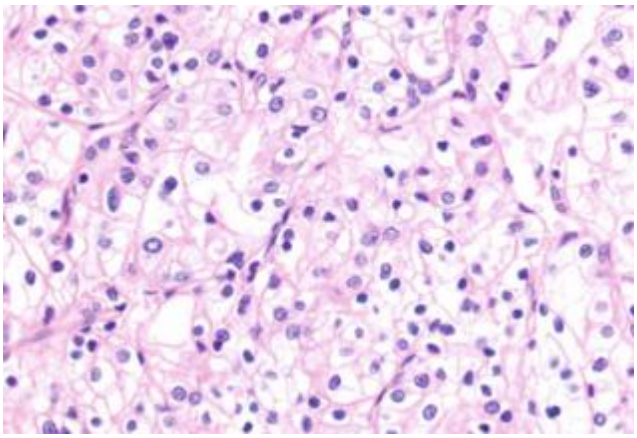
Fuhrman grading was first described in 1982.It is the most commonly used grading system for RCC. It depends on the nuclear size and shape, chromatin and nucleolar prominence. It is categorized into G1–G4.It is an independent prognostic predictor for RCC . Grade 1 and 2 may be taken together as low grade because they are not behaving different in terms of prognosis in multivariate analysis. But grade 3 and grade 4 tumors must not be grouped together because the former have better 5-year cancer-specific survival than the later.

GRADE	NUCLEAR SIZE µM	NUCLEAR SHAPE	CHROMATIN	NUCLEOLI
1	< 10	ROUND	DENSE	NOT VISIBLE
2	10-15	ROUND	FINE GRANULAR	SMALL
3	15-20	ROUND/OVAL	COARSE GRANULAR	PROMINENT
4	>20	PLEOMORPHIC	HYPERCHROMATIC	LARGE

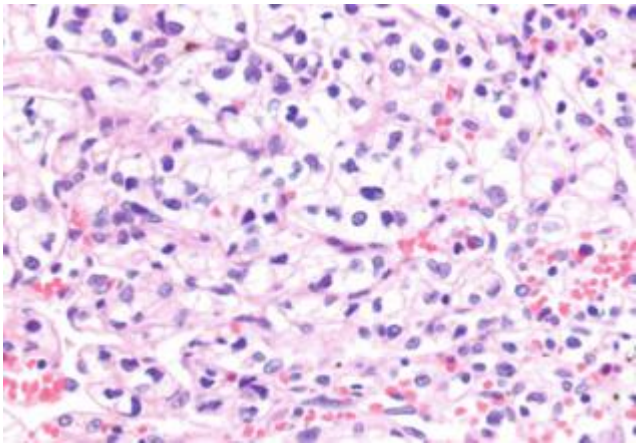
The 5 year CSS for grade III and grade IV are 45–65% and 25–40% respectively.The prognostic value of Fuhrman grading for nonclear cell RCC, however, remains controversial.There is no statistical significance for papillary ca in multivariate analysis.Of all the parameters the nucleolar features gain importance.It is associated with survival in both univariate and multivariate analyses.



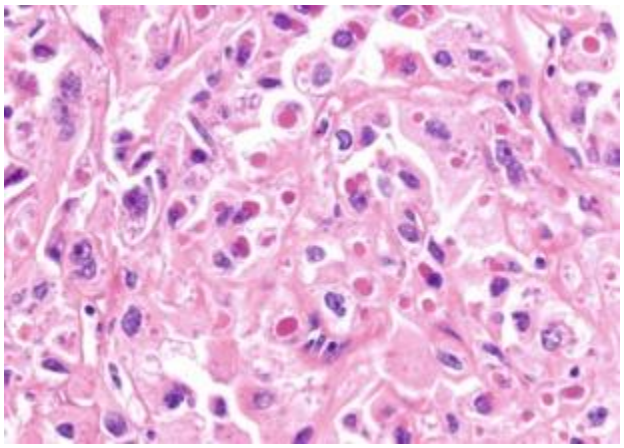
. FUHRMAN GRADE I



FUHRMAN GRADE II



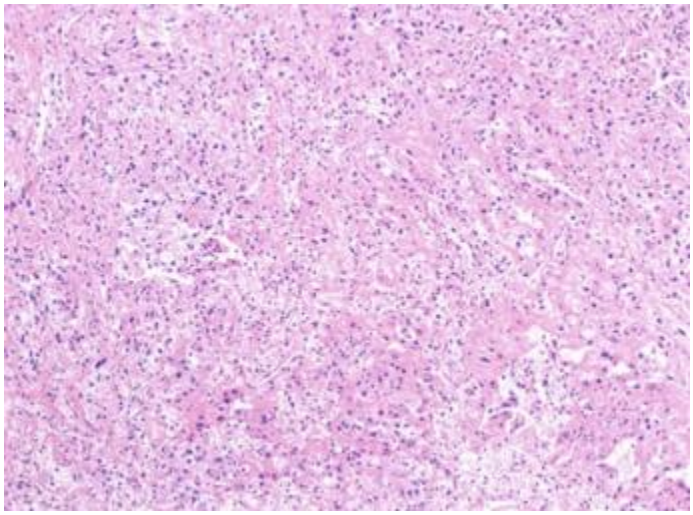
FUHRMAN GRADE III



FUHRMAN GRADE IV

Sarcomatoid Differentiation

Sarcomatoid differentiation is present in about 5% of RCCs and can be observed in any RCC subtype . So the sarcomatoid RCC is now not considered a distinct subtype of RCC by 2004 WHO classification. It is a presentation of a high-grade and poorly differentiated component. RCC with sarcomatoid differentiation typically will have other adverse features, which include large tumor size, perinephric fat and vessels extension, and presence of hemorrhage and necrosis. The patients usually present with distant metastasis and there is an increased risk of cancer-specific death. It is a poor prognostic indicator in univariate and multivariate analyses .Usually this sarcomatoid differentiation is given a Fuhrman grade 4 by the pathologists. Sarcomatoid components will appear as bulging, lobulated areas with white to gray and it has a firm and fibrous cut surface .



SARCOMATOID DIFFERENTIATION

Histologically, there are malignant spindle cells with resemblance to leiomyosarcoma, fibrosarcoma, angiosarcoma, rhabdomyosarcoma. So the existing RCC which may be clear cell, papillary, chromophobe RCC and sometimes collecting duct RCC are mentioned with sarcomatoid differentiation. However, if any of the subtypes could not be possible and if the sarcomatoid component overruns RCC epithelial components,which is a rare occurrence, then the possibility of a primary sarcomatoid carcinoma arises. Rhabdoid differentiation is in approximately 5% of RCCs with large eccentric nuclei, macronucleoli and prominent acidophilic globular cytoplasm . It is associated with high grade and stage with extrarenal extension. It is a marker of high risk for metastasis and adverse prognosis even when the rhabdoid component is minimal .

Tumor Necrosis

In Clear Cell RCC ,when tumor necrosis is identified macroscopically or microscopically,it is a poor pathological factor and is associated with adverse clinical outcomes in both univariate and multivariate analysis. Mayo Clinic study clearly depicts that histological necrosis is associated with twice the CS Death rate compared to those without necrosis . Two nomograms ,SSIGN from Mayo Clinic, and nomogram from MSKCC, both incorporate tumor necrosis . The extent of necrosis has a good correlation with the cancer specific death rates.In non clear cell RCC the role of tumor necrosis in prognostication is limited.

Microvascular Invasion

Microvascular invasion is defined as tumor cells invading the vessel wall or neoplastic emboli in the intra tumoral vessel detected microscopically. This is present in 13.6–44.6% of RCC. RCC of high stage and grade usually have microvascular invasion. The prognostic role in RCC is controversial. But there are several studies that demonstrate that MVI may have an independent predictive role for cancer-specific mortality or disease recurrence.

Imaging

PLAIN RADIOGRAPHY

Plain radiographs are the imaging techniques before the era of ultrasound or computed tomography (CT) or MRI. Usually RCC is not seen on a plain x ray but on rare occasions it may be seen .It appears as an space occupying lesion that is irregular.It distorts the normal appearance of the renal shadow.15% of RCC has calcifications which can be identified on a plain X ray KUB. The calcification can be thin peripheral rim calcification or irregular central calcification, or it can be a combination. When there is a calcification in the periphery which appears thin then the probable diagnosis are 80% benign cysts, 20% cystic renal malignancies. On the other hand the renal masses which are containing central, irregular calcification are the ones which are malignant (87%). A calcification in both the centre and the

periphery of a renal mass makes the proabablity of renal mass to be malignant by 50%.

Lytic skeletal abnormalities which are due to hematogenous spread can be seen. When the growth of the lesion is slow and when there is a bubbly appearance on a X ray , there are more chances of malignancy due to the metastasis.Plain X ray of the skull and the spine should be taken in case of RCC associated with Tuberous sclerosis because of the associated Skull and spine osteomas.

INTRAVENOUS UROGRAPHY

Intravenous urography (IVU) is used to investigate the nature of a renal mass lesion and the proportion of normal functioning segment of the uninvolved kidney. Nowadays when investigations such as CT and MRI are available, IVU is becoming less popular.IVU is usually performed in the following way. A scout abdominal or KUB radiograph is first taken and then 40 mL of contrast administration over 30 s. Any calcification is to be looked for in the pilot film and the bowel gas should be noted before the contrast administration.

RCC is an expansile and an exophytic mass that alters the normal contour and it displaces the normal renal structures. RCC produces calyceal splaying and stretching ,with destruction of the calyces.Occasionally, an exophytic RCC can cause no effect on the calyceal system. When RCCs are located in a direction that

is above or below the kidney there may be a hinderance to locate the lesion with IVU, because the lesion can be masked by the overlying pelvicalyceal system and the nephrogram from the normal kidney. Other supportive evidence that can be seen in a IVU that are diagnostic of RCC is the pelvic notching .It occurs due to enlarged pelvic vessels at the pelvi uretric junction where there is an increased blood supply to a RCC.

ULTRASOUND

The Renal ultrasound with Doppler is the cost effective modality and most of the renal masses are easily picked up by an ultrasound abdomen imaging .The ultrasound has the ability to differentiate whether the content is solid or fluid and hence when the diagnosis of the renal masses are made as simple cysts there will be no further diagnostic evaluation .Echogenicity, vascularity , invasion into adjacent structures and calcification are the features that are to be looked for in an ultrasound examination. On ultrasound, RCCs are seen as a single or multifocal mass that are exophytic but they are not diagnostic. These masses may be either hypoechoic, isoechoic, or hyperechoic when compared with that of the normal renal parenchyma.When there are heterogenous echoes in a cystic lesion a diagnosis of RCC should be suspected.

About 33 % of RCCs are hyperechoic , but when size of an RCC is small and it is not a classical hyperehogenicity on Ultrasound, a diagnosis of angiomyolipoma should be made and proceeded with definitive investigations. When there is a mass with an anechoic perimeter or cystic areas internally ,on USG examination, they suggest RCC, and a CT or MRI is further required for evaluation.RCC has intra tumoral fat when there is a tumor encasement of the perirenal or renal sinus fat. Ultrasound has the ability to show the internal architecture of renal tumors. This feature is very useful when lesions which are equivocal (neither the lesion is benign or purely malignant) on CT or MRI .It may demonstrate the septa and can say whether there are solid elements in the periphery of the renal mass lesion so that when these features are present a diagnosis of a malignancy can be done with a probability. Ultrasound is used to detect the features that are due to the infiltration of the surrounding structures by RCC such as hydronephrosis . When there is an encasement of the renal vessels by RCC there is diminished blood flow to the area that is involved and that can be picked up by a Doppler scan. An RCC that is infiltrating sometimes ,may cause only minimal abnormalities or none . Doppler examination is a specific test to look for the renal vein thrombus and IVC thrombus but the extent of thrombus should be made by MRI/Echocardiogram or a transesophageal echo. Staging of

RCC and hilar lymphadenopathy detection is limited by the ultrasound examination.

COMPUTED TOMOGRAPHY

A thin slice CECT scan is the most important diagnostic test used in the diagnosis of a renal mass .A renal mass that enhances by more than 15 HU after the contrast administration is to be considered an RCC until proved otherwise. Solid mass lesions with attenuation of less than – 20 HU are due to the presence of fat and are diagnostic of angiomyolipoma .The new technique of multidetector row computed tomography (MDCT) allows the formation of high quality images with a good resolution and also the scanning time is much more faster , and multiphase images are taken. The data getting times is usually very short with the MDCT because they have short gantry rotation time usually 0.5 seconds.It is usually combined with many detectors so that it provides increased coverage along the z axis. Retrospectively, with this MDCT, different multiplanar images and 3D format imaging with minimal artifacts can be done this is made possible by very small section data reconstruction with anusual isotropic data is also obtained. So the total kidney can be imaged in less than 10 seconds . Renal vasculature imaging and collecting system imaging can be done with the help of this multiphase imaging. This is most important when a nephron sparing surgery is planned.

The precontrast image in a CT scan is also important because by this, a diagnosis of a hyperdense cyst can be made. Corticomedullary images gives greater detail in the assessment of renal vessels, tumor vascularity, and the involvement of the venous system by the lesion. In the corticomedullary phase contrast is present in the small blood vessels in the cortical region , the cells surrounding the tubules, proximal tubules, and in the columns of Bertin. So the correct time of the corticomedullary phase depends on the speed and volume of contrast that is injected, and the patient's heart rate and the cardiac output. The next phase is the nephrographic phase . It occurs when the contrast moves further down the tubules.It is during this phase, there is homogeneous enhancement in the kidney. Here the lesions that are situated in the medulla also enhance well. So this phase is the best phase for the identification of small renal masses .

The next phase is the excretory phase which begins when the contrast is secreted into the pelvicalyceal system, approximately 5 min after contrast administration.In this phase, the nephrogram is still homogeneous but its measurements in terms of HU is minimised. When the mass is located centrifugally,and when there is an involvement of the pelvicalyceal system the image should be taken in this phase for better diagnosis.

There are some pitfalls in the measurement of HU in the CT scan. Due to feature called beam hardening, the HU can move slightly above the normal value

because of the contrast enhancement in the normal renal tissue that is located nearby. This increase in the value is more pronounced when the lesions are small ,that are located intrarenally.

Although minimal areas of enhancement can be taken into consideration for the diagnosis, the lesions with no definitive change after contrast or if there is a change in HU by less than 20 HU it should be considered as an indeterminate mass and further evaluation with MRI must be done.So in small lesions MRI has to be used for equivocal contrast enhancement. The time taken for the persistence of contrast enhancement in case of renal masses is minimal.So the washout time from the mass can be studied by the use of an MRI. A study has suggested that the measurement of the washout of contrast from the mass at 15 min shows the ability to differentiate between renal neoplasms and hyperdense cysts.

MAGNETIC RESONANCE IMAGING

The most peculiar feature and the most advantageous one with MRI over other imaging modalities is that it produces good images of the soft tissue and scanning can be done in the axial, coronal and the sagittal sections. With the use of MRI, the T staging in the malignant renal masses are made and therby appropriate management can be planned. When the use of contrast has been contraindicated in case of chronic renal failure or contrast allergy,MRI is the test that is useful

.Patients who have a solitary functioning kidney and those who need repeated CT to be done for follow up, can be followed up with MRI. This benefits the patient both from the effects of radiation and the dose of contrast that is frequently used which may precipitate renal failure in these patients.

The MRI scan should be taken by asking the patients to hold their breath.Nowadays respiration gated MRI have also come into vogue that are more breath friendly. The following sequence of images are taken (a) a T1 image with in and out of phase.This is helpful for the detection of fat because there will be signal loss in out of phase images (b) T2-weighted image in axial or coronal planes.This best gives the anatomy of the renal mass, the relationship of the mass to the renal pelvicalyceal system and the features of the mass that are probably malignant (3) a dynamic contrast enhanced T1 image.

For the contrast pictures, the pictures are usually obtained before and after contrast administration during the arterial, corticomedullary, and nephrographic phases. As mentioned previously, on all these phases, the nature of the mass can be studied.Multiple thin slices of films should be taken and that too the images are to be taken in the saggital and coronal views so that they give a better idea about the location of the mass to the collecting system and the adjacent retroperitoneal structures. If a nephron sparing surgery is planned then the pictures are to be taken in an arterial phase so that the normal renal tissue supplied by the vessels should be

identified and that should be spared. During the phase of contrast excretion from the collecting system, the pictures should be taken in the coronal plane to obtain the whole urogram view. It is during this excretory phase the presence of venous thrombi can be seen.

RCC is usually seen as hypointense or isointense on T1-weighted images. They are heterogeneously hyperintense on T2-weighted images. RCC readily enhances with contrast gadolinium. The above mentioned clauses have exception and they may be of any intensity. The enhancement of a renal mass is less than that of the normal renal parenchyma and it should be looked in T 1 images. When there is a small amount of fat in RCC there will be signal loss when out of phase images are obtained. So whenever there is a signal loss in an RCC there should not be a hurry in the diagnosis of an AML. The fat in RCC may be due to the osseous metaplasia or due to the engulfment of the renal sinus fat by the tumor. When there is an irregular thickening in the wall of a cystic lesion or nodules or when there is an enhancement there is a suspicion that the mass is malignant.

DIFFUSSION WEIGHTED MRI

Brownian motion or the movement of the water molecules forms the basis of the diffusion weighted MRI. It is the restriction to the movement of protons in the water molecules.This depends on the environment ,where the protons are situated

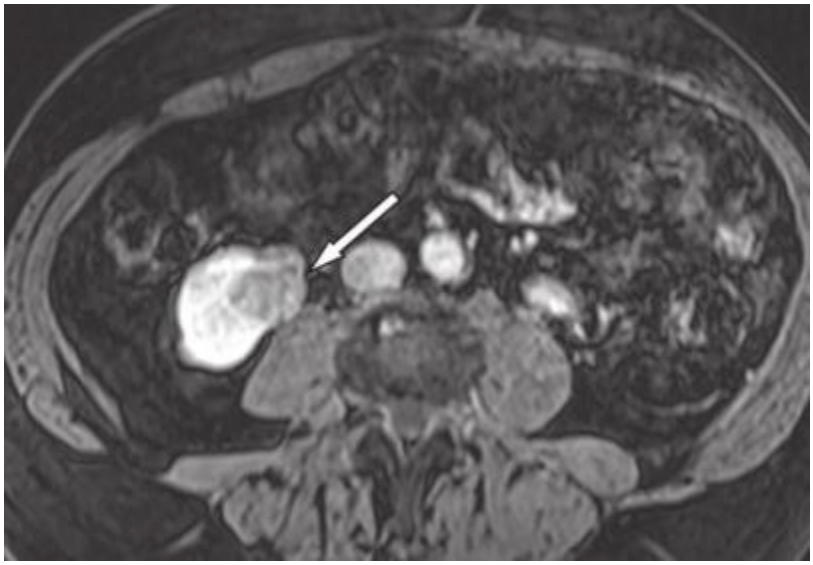
in the renal masses, which are both qualitatively and quantitatively assesed.In tumors which are highly cellular and which has higher density of cell membranes there is restricted motions of proton molecules.This restricted motion of protons is seen as high signal intensity on DWI images with a corresponding low apparent diffusion coeffiecient value (ADC) , which measures the quantitative value of the MR imaging.DWI is used in clinical practice by measuring the signal intensity and the ADC value of the normal renal parenchyma and the lesions.Quantitative values are being examined by several researchers for distinguishing between the benign and malignant character of the renal neoplasms.

Diffusion-weighted imaging (DWI) is most commonly used in brain.Initial studies that has been conducted had shown great accuracy in the depiction of lesions as cerebral stroke, malinancy, diseases due to bacteria and viruses and metabolic conditions .Due to the inherent extreme sensitivity to motion which is from breathing and bowel movements and artefacts, which results in a high signal to noise ratio , the role of DWI is limited to the cranial cavity.But because of the advances in MR imaging and the use of quick sequences in MRI good quality images is being obtained in abdominal imaging .

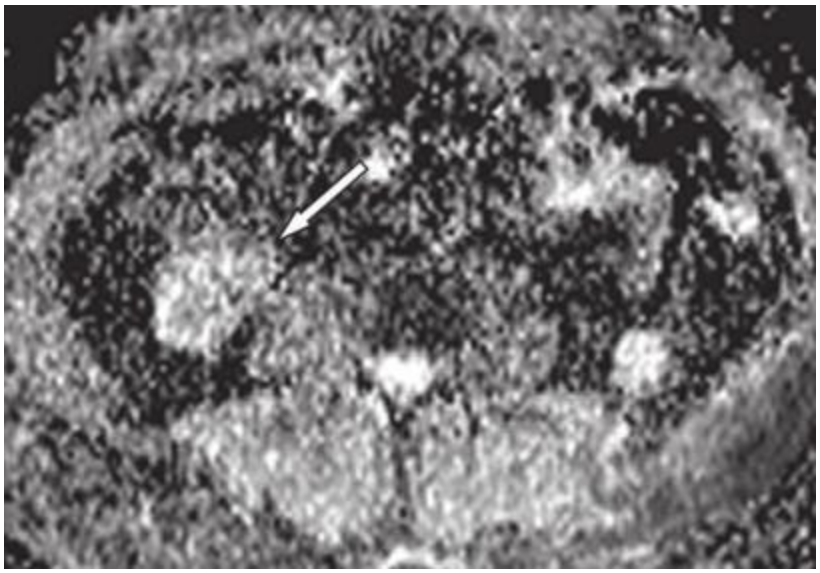
The management for the RCC should be appropriate and hence it is important to diagnose that the mass is actually benign or malignant.So there is a need for the ADC values in case of a renal mass so as to make a diagnosis when

the contrast cannot be administered and in case of indeterminate mass.The ADC value was high in simple renal cysts and renal pelvis of hydronephrotic kidney because of the high levels of diffusion .In case of malignancy ,where there is a low level of diffusion, there will be low ADC value. Cellular lesions such as RCC will have higher b value when compared with normal renal parenchyma.So in diffusion weighted imaging, the ADC values are compared using b values of 0,400,800.

The role of the ADC value in characterising the histological subtypes of renal carcinoma is limited in previous studies. It will also differentiate the grade of the tumours as the high grade tumours will show restricted diffusion. Therefore, the present study aimed to evaluate the role of DWI in combination with T 1 and T 2 weighted MRI for the characterisation of renal carcinoma.



A MRI of a right renal mass



Diffusion weighted MRI mass showing restricted diffusion with increased signal intensity and low ADC value.

MATERIALS AND METHODS

STUDY DESIGN

Prospective cross-sectional diagnostic study

PLACE OF STUDY

The study was conducted in the Department of Urology, Madras Medical College and Rajiv Gandhi Government Hospital, Chennai- 3.

ETHICAL CLEARANCE

The institutional ethical review board at our hospital approved the study.

(No 10062013)

INCLUSION CRITERIA

All newly diagnosed cases of renal masses

EXCLUSION CRITERIA

1. Patients with Renal masses less than 2 cm.
2. Previously received chemotherapy or radiotherapy for renal masses.
3. Prior diagnosis of TCC pelvis.

METHOD OF STUDY

Informed consent obtained from all the patients after explaining details of the study. All details were recorded in a proforma as an inpatient procedure. Analysis was done with the collected details prospectively.

PATIENT EVALUATION

All cases of renal masses will be evaluated by clinical examination, renal function tests, S.calcium ,E.S.R ,Complete haemogram,LFT, CXR ,imaging studies in the form of USG with Doppler / CECT KUB.

MRI

MR Imaging

MR imaging was performed with 1.5-T clinical MR systems (Magnetom Siemens Medical Solutions, Germany) by using body phased-array coils using eight elements . The routine renal mass MR imaging protocol included the use of getting the images in T1 in and out of phase using respiration gated techniques.A second coronal T2 image breath hold half Fourier single shot turbo spin echo sequence was taken.Three different breath-hold DW image acquisitions was performed in the transverse plane by using a fat suppressed single shot echo planar imaging sequence with tridirectional gradients and three sets of b values: 0, 400, and 800 sec/mm 2 .

ADC CALCULATIONS

ADC mapping is done at the console of the MRI . With linear regression analysis of function , the ADC value was calculated. All renal masses with a maximal size more than 2 cm were precisely characterised on basis of signal intensity on T1- and T2-weighted images and image subtraction . Cystic renal lesions are classified according to the Bosniak classification system . Fat-containing AMLs were diagnosed by the standard criteria based on findings at in phase and out of phase T1 weighted imaging. Hence renal lesions were diagnosed to be benign or presumably malignant .

The mean ADC values of the lesions found on MRI were measured by using regions of interest . An average of two or three measurements per lesion is done , which depends upon on the size of the lesion. The regions measured has a mean size of about 4 cm that were round or oval, depending on the size of the lesion. In all patients, the region of interest included the entire lesion and we left the necrotic area of the renal mass.

The ADC values of the normal kidney in the both the renal cortex and the medulla were measured in three locations (upper, middle,and lower poles) of the kidney (one kidney in cases of prior nephrectomy) . The measured regions

of interest were about 1–2 cm in diameter, and measurements from all patients were taken and the mean was found out.

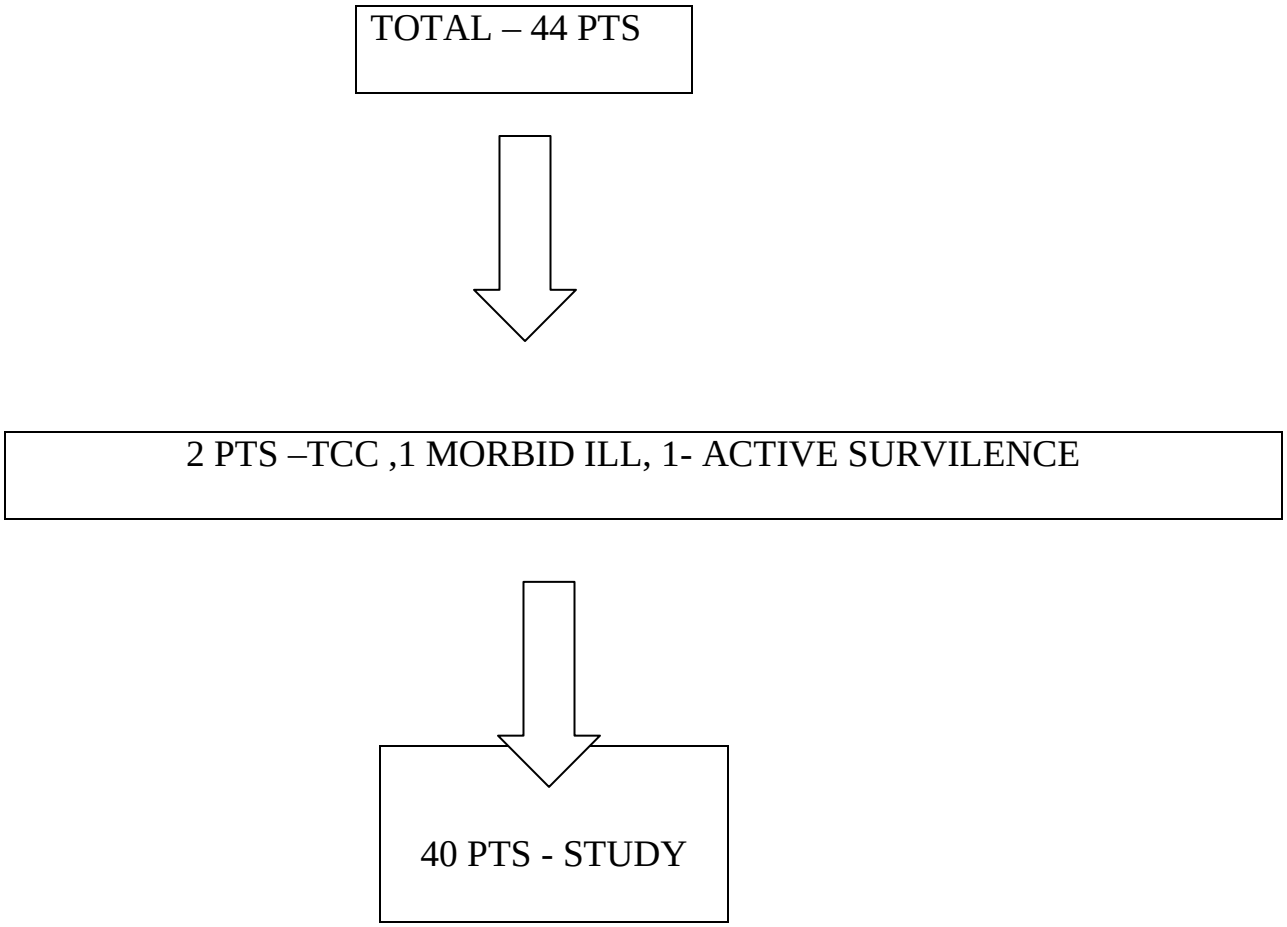
All malignant and benign lesions were confirmed at histopathologic examination after partial or total nephrectomy. Diffusion weighted Magnetic Resonance Imaging of KUBU region will be taken at the time of hospital admission. The tumor ADC Values and the values from the kidney was noted. The patients are taken up for radical/simple nephrectomy. These results will be correlated with Clinical, Imaging and the pathological finding.

STUDY ANALYSIS

The Statistical Package for the Social Sciences, version 18.0.2 (SPSS) was used for the statistical analysis. A p value equal to or below 0.05 was considered significant.

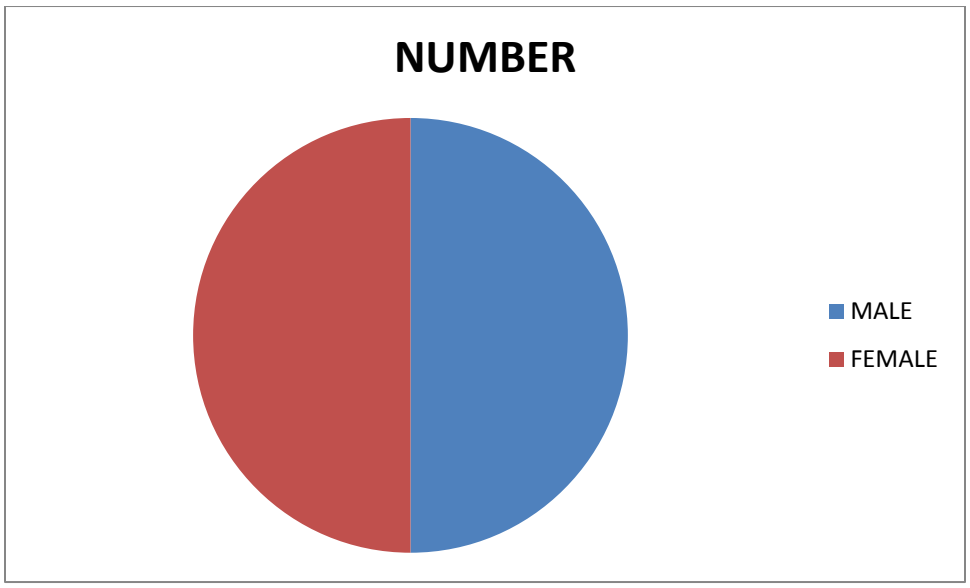
RESULTS

Our study consists of about 44 patients of which four did not meet the inclusion criteria. One pt was morbidly ill, so a histopathological examination could not be obtained . Two cases of TCC pelvis were diagnosed preoperatively and were excluded in the study. In one case, the size of the renal mass lesion was 2 cm and was excluded from the study as the patient opted for active surveillance.



PATIENTS CHARACTERSTICS

GENDER DISTRIBUTION IN THE STUDY POPULATION



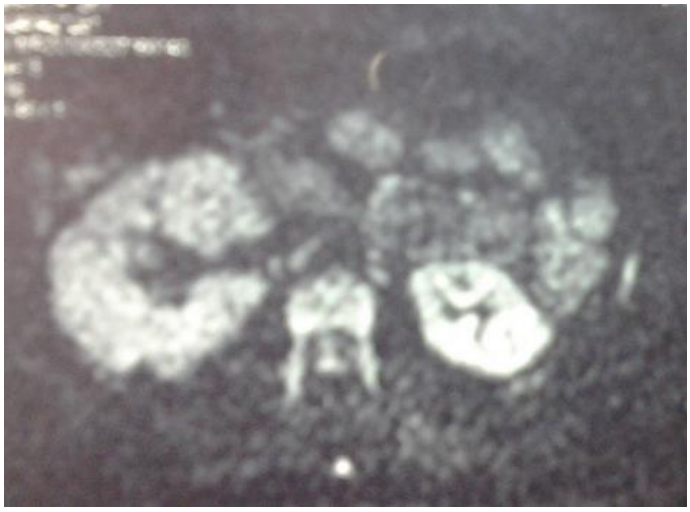
There were twenty males and twenty females in the study population.

Equally distributed of about 50% in the study.

AGE DISTRIBUTION

	N	Minimum	Maximum	Mean	Std. Deviation
Age in years	40	35	81	53.98	10.726

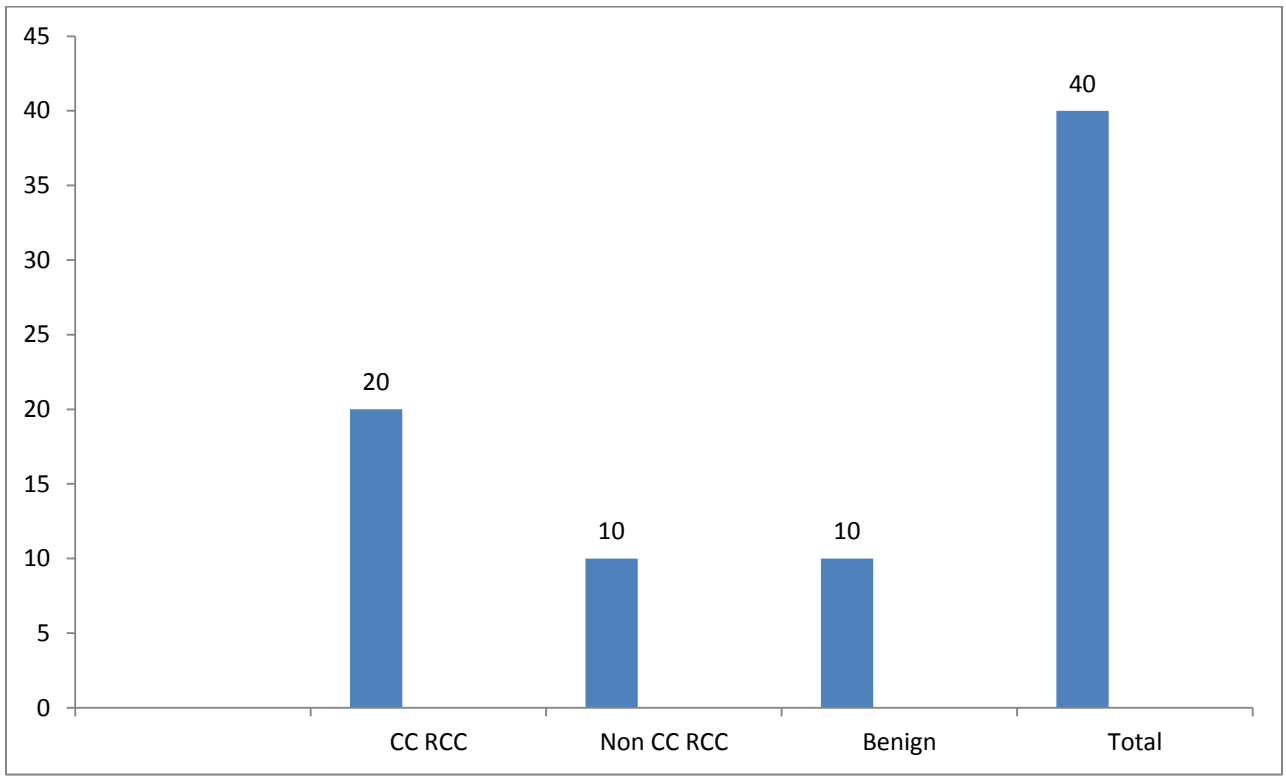
DIFFUSION WEIGHTED MRI IMAGES OF PATIENTS WITH RENAL MASSES



Right renal mass with DWI . ADC VALUE – 1.32 x $10^{-3}MM^2/S$

RIGHT RENAL MASS DWI .ADC VALUE – 1.64 x $10^{-3}MM^2/S$

HISTOPATHOLOGY REPORTS



From the 40 nephrectomised specimens ,the clear cell RCC cases were about 20 , non clear cell RCC were 10 and benign pathology were 10.

Of the thirty cases of malignancy, 3 cases were T1 and 8 cases were stage T2 and 19 cases in stage T3. The mean size of the renal masses were 11.56 cm .

MEAN ADC VALUE OF THE RENAL MASSES

	N	Mean	S.D	Std. Error	95% Confidence Interval for Mean		Min	Max
					Lower Bound	Upper Bound		
CC RCC	20	1.2765	.09511	.02127	1.2320	1.3210	1.12	1.44
Non CC RCC	10	1.6880	.08651	.02736	1.6261	1.7499	1.53	1.81
Benign	10	2.4260	.43257	.13679	2.1166	2.7354	1.68	2.84
Total	40	1.6667	.52473	.08297	1.4989	1.8346	1.12	2.84

The mean ADC value of the clear cell RCC group is 1.27 X $10^{-3}mm^2/s$.

The mean ADC value of the Non Clear cell RCC is 1.68 X $10^{-3}mm^2/s$.

The mean ADC value of the benign renal masses in our study is 2.42X $10^{-3}mm^2/s$.

So the cut off ADC value for diagnosing all malignant vs benign lesions would be less than 1.74X $10^{-3}mm^2/s$.and the ADC value for diagnosing clear cell vs non clear cell lesions would be 1.32 X $10^{-3}mm^2/s$ (using 95 % confidence limits)

COMPARISION OF ADC VALUE BETWEEN THE GROUPS

(I) HPE Report	(J) HPE Report	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
CC RCC	Non CC RCC	-.4115(*)	.08830	.001	-.6271	-.1959
	Benign	-1.1495(*)	.08830	.001	-1.3651	-.9339
Non CC RCC	CC RCC	.4115(*)	.08830	.001	.1959	.6271
	Benign	-.7380(*)	.10196	.001	-.9869	-.4891
Benign	CC RCC	1.1495(*)	.08830	.001	.9339	1.3651
	Non CC RCC	.7380(*)	.10196	.001	.4891	.9869

The mean values compared between the other groups that is between the malignant and the benign and the clear cell and the non clear cell group are statistically significant.

Comparison of histological grades between the clear cell RCC groups

The mean ADC value cut off for diagnosing a high grade RCC is

1.23 X $10^{-3}$$mm^2$/s.(95 % confidence limits)

COMPARISION OF ADC VALUE BETWEEN THE CLEAR CELL RCC GRADES

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
II	6	1.3933	.03882	.01585	1.3526	1.4341	1.34	1.44
III	10	1.2580	.03360	.01062	1.2340	1.2820	1.21	1.32
IV	4	1.1475	.02754	.01377	1.1037	1.1913	1.12	1.18
Total	20	1.2765	.09511	.02127	1.2320	1.3210	1.12	1.44

MULTIPLE COMPARISIONS BETWEEN THE GRADES OF CLEAR CELL RCC

(I) CC RCC	(J) CC RCC	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
II	III	.1353(*)	.01770	.001	.0899	.1807
	IV	.2458(*)	.02212	.001	.1891	.3026
III	II	-.1353(*)	.01770	.001	-.1807	-.0899
	IV	.1105(*)	.02028	.001	.0585	.1625
IV	II	-.2458(*)	.02212	.001	-.3026	-.1891
	III	-.1105(*)	.02028	.001	-.1625	-.0585

COMPARISION OF T STAGING AND THE ADC VALUE

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
T1	3	1.5633	.24664	.14240	.9506	2.1760	1.28	1.73
T2	8	1.3838	.17054	.06030	1.2412	1.5263	1.18	1.76
T3	19	1.4026	.23168	.05315	1.2910	1.5143	1.12	1.81
Total	30	1.4137	.21720	.03966	1.3326	1.4948	1.12	1.81

STAGING AND ADC VALUE SIGNIFICANCE

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.077	2	.038	.802	.459
Within Groups	1.291	27	.048		
Total	1.368	29			

There is no statistical significance between the T stage and the ADC value

DISCUSSION

RCC is usally diagnosed by CECT KUB or contrast MRI scan.But when there is an extensively necrotic or renal mass that is cystic in appearance, this may have minimal enhancement , and the diagnosis of a tumor and a benign complex cyst may overlap .

So to avoid these circumstances diffusion weighted MRI has come into vogue nowadays to establish a reliable diagnosis.This diagnostic imaging is proved beyond doubt in neurosurgery in establishing the diagnosis. The practical value of the imaging is that, it is used to differentiate between the tumors and ischemia which occurs in acute stroke patients.

Similarly Namimoto has found that the ADCs of malignant masses is significantly lower than the ADCs of benign lesions of the liver. Investigators from other studies also show that there is a different ADC value for hepatic metastases, hepatic hemangiomas, and hepatocellular carcinomas .

Our study results state that the renal mass lesions has different ADC values for different lesions because of the change in tissue contents.This different ADC values are due to the different diffusion characterstics in renal mass lesions.The necrotic or cystic tumor areas have higher ADC values than that of the solid tumor tissue. The T1 signal appearances of a lesion is also related to the ADC values of

the lesion. So T1 hypointense cysts have higher ADC value than T1 hyperintense cysts, and viceversa. The reason for the association between T 1 and the ADC value is not known. This may be due to the presence of either high protein content in the cyst or blood in the cyst that leads to high T1signal in the mass lesions.

Benign renal mass and necrotic or renal tumor areas have significantly different ADC.This is because ,in the unhealthy, avascular necrotic s tumors there is restricted water diffusion unlike the cystic renal masses like hydatid cyst,hydronephrosis. So, the ADC value can be used as a supportive and an important marker for characterizing renal mass lesions.

Squillaci , in a study which included benign and malignant cystic mass lesions ,have shown results similar to our study. The mean ADC value of the RCC masses were 1.7 $x10^{-3}$ mm^2/s and that for simple cysts mean ADC was 3.65 $x10^{-3}$ mm^2/s thus demonstrating a significantly higher value for the benign cystic masses.

Zhang has studied the DW MRI imaging to evaluate 25 Cystic and solid renal mass lesions. Larger areas of interest was taken by them for the measurement of the ADC value.Their ADC measurement represented the entire mass.Thereafter, based on the contrast-enhanced MR report, they divided the lesion into solid and cystic necrotic parts. Zhang had the report of lower ADC value in the intra cystic necrotic portions of neoplasms when compared to the

ADCvalue in simple cysts.Their study did not mention the differences in ADC based on histology subtype of RCC. In our study, we measured the ADC in the entire mass lesion (in two to four images so that it covers the entire lesion) as well as the cystic and solid portions of cystic RCCs.

In our study, the mean ADC value of high grade tumors (Fuhrman grade III & IV) were significantly lower than that of low grade tumors in the clear cell RCC group. This is because of the restricted diffusion in the high grade tumors .Thus ADC value could also add to the prognosis of tumors when the grade of the tumors is determined.

In our study, in one case, even though there was a high signal in T1 there is higher ADC value due to the non restricted diffusion of the molecules in the simple cyst and the ADC value correlated with the HPE report. Different considerations have to be made for clear cell carcinoma and non clear cell carcinoma.In the non clear cell carcinoma ,these tumors form trabecular structures, nests and tubular formations containing large interstitial spaces where there is water and molecules can move freely. In our study, the mean ADC values of clear cell carcinoma and non clear cell carcinoma were 1.27 $x10^{-3}$ mm^2/s and 1.68 $x10^{-3}$ mm^2/s respectively .On data analysis they were found to be statiscally significant. .

A meta-analysis of 99 studies was done previously to know whether all renal tumours that are diagnosed should be subjected to surgical management. It stated that active surveillance can be done in selected cases so that there is no intermediate survival benefit when surgical modalities are considered.There is no increase in the local recurrence when the patients are under surveillance. The study had a good follow up period of about 4 years. So based on this results we can suggest that when there is a role for surveillance,where the histology and the grade of the tumor is to be known preoperatively, this specialized MR imaging can be done.

Also for the start of the targeted therapy, the histology of the RCC should be known in the case of metastatic disease. Sunitinib is more effective in clear cell RCC and it is the first line drug ,whereas the mTOR inhibitors like Temsirolimus is used for non clear cell RCC.

The mean value of angiolipomas in our study is $1.83x\ 10^{-3}mm^2/s$.

This ADC value differs from that of the other benign renal mass lesions of the kidney . Angiomyolipoma, as known, is composed of differing amounts of smooth muscle, fat and good vasculature with a significant cellularity .Because it also has with it, a collagenous interstitial stroma ,which reduces water diffusion velocity, the ADC values in the renal mass lesion is low than that of other benign

lesions. But the diagnosis of AML can be made readily on MRI with in and out of phase sequencing imaging.

When there is a lowered creatinine clearance ,where the contrast cannot be used, there arises a difficulty in the differentiation whether it is hydronephrosis or pyonephrosis, which utilizes the DW MRI .This has been investigated in prior studies .

Currently, MRI is considered the only imaging modality which is capable of measuring in vivo diffusion of molecules. Because of its high blood flow and basic function of fluid management , that justify high ADC values, the kidney is an ideal organ for DWI MR. The mean ADC value of normal renal parenchyma was 2.34±0.12 x 10 -3 mm 2 /sec .The variability of different ADC values is due to different MR techniques, and the different diffusion weightings used for the imaging sequence, which is denoted by the b factor value, encompassing the main characteristics of diffusion gradients (amplitude, duration and time interval between gradients).

The ideal diffusion weighting of an echoplanar sequence is still not conclusive by the experts. When the low b factor values (30-100 s/mm 2) are used, the perfusion of the microcircle and the T2 tissue components ,there will be an overestimation of ADC values. Contrarily , the use of high b factor values (>1000

s/mm 2) there will be more noisy images due to the low MR signal which is due to the short T2 time.So in our study the diffusion weighted imaging sequence is the average of three b values thereby reducing the errors in measuring the ADC value.

One limitation of the study was that the study did not evaluate the tumor cellularity in histopathological report.

CONCLUSION

In conclusion, our study states that Diffusion weighted MR imaging can be used in the management of renal masses, more so to differentiate between benign mass lesions from renal cell cancer.

The histologic subtype of RCC can be diagnosed pre op from the ADC values and can guide targeted therapy.

It also establishes the grade of the tumor in clear cell RCC thereby prognosis of the disease is known.

When the use of contrast is contraindicated, such as gadolinium, there is a role for DWI in the diagnosis of malignant renal masses.

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APPENDIX I

INFORMED CONSENT FORM

Title of the study:

DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN RENAL MASSES

Name of the Participant:

Name of the Principal Investigator: Dr. MOHANKUMAR.D

Name of the Institution: Rajiv Gandhi Govt.General Hospital, Chennai -3.

Documentation of the informed consent

I _____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in

DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN RENAL MASSES

1. I have read and understood this consent form and the information provided to me.

2. I have had the consent document explained to me.

3. I have been explained about the nature of the study.

4. I have been explained about my rights and responsibilities by the investigator.

5. I have been informed the investigator of all the treatments I am taking or have taken in the past 3 months including any native (alternative) treatment.

6. I have been advised about the risks associated with my participation in this study.

7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.

8. I have not participated in any research study within the past 6 month(s)

10. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.

11. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.

12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.

13. I have understand that my identity will be kept confidential if my data are publicly presented

14. I have had my questions answered to my satisfaction.

15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

For adult participants:

Name and signature / thumb impression of the participant (or legal representative if participant incompetent)

Name _____ Signature_____

Date_____

Name and Signature of impartial witness (required for illiterate patients):

Name _____ Signature_____
Date_____

Address and contact number of the impartial witness:

Name and Signature of the investigator or his representative obtaining consent:

Name _____ Signature_____
Date_____

APPENDIX II

TITLE:DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN RENAL MASSES

PROFORMA

NAME:

AGE:

SEX:

IP NO:

PRESENTING COMPLAINTS:

BASIC INVESTIGATIONS:

USG KUB:

CECT KUB:

DIFFUSION WEIGHTED MRI:

PROCEDURE DONE:

POST OP HPE REPORT:

APPENDIX III MASTER CHART

S.NO	NAME	AGE/SEX	IP NO	DIAGNOSIS	STAGE	ADC VALUE	PROCEDURE	HPE REPORT
1	KANNAN	63/M	113662	LT RENAL MASS	T3aN1M0	1.13	LT RAD NEP	CC RCC GRADE 1V
2	JEYARAMAN	60/M	79111	RT RENAL MASS	T3bN1M0	1.26	RT RAD NEPH	CC RCC GRADE III
3	PATCHAIAMMAL	81/F	55442	RT RENAL MASS	T2N0M0	1.32	RT RAD NEPH	CC RCC GRADE III
4	VALLIYAMAL	45/F	32614	LT RENAL MASS	T2N0M0	1.34	LT RAD NEPH	CC RCC GRADE II
5	PARVATHY	40/F	22234	RT RENAL MASS	T3aN1M0	1.53	RT RAD NEPH	CHROMO GRADE II
6	CHINNAPILLAI	50/F	12347	RT RENAL MASS	T3AN0M0	1.23	RT RAD NEP	CC RCC GRADE III
7	VEERABATHIRAN	49/M	17112	LT RENAL MASS	T3aN0MO	1.43	RT RAD NEP	CCRCC GRADE II
8	SRINIVASAN	48/M	92357	RT RENAL MASS	T2N0MO0	1.36	LT RAD NEP	CC RCC GRADE II
9	KRISHNAVENI	60/F	87124	LT RENAL HYDATID CYST		2.52	LT NEPH	HYDATID CYST
10	SATHYA	43/F	66164	LT XGPN		2.78	LT NEPH	XGPN
11	VEERARAHAVAN	59/M	72343	RT METS RCC	T3aNOM1	1.76	RT CYT NEPH	UNCLASSIFIED RCC III
12	SANJEEVAMMAL	44/F	11185	RT RENAL HYDATID CYST		2.74	RT NEPH	HYDATID CYST
13	MUTHUSWAMY	77/M	79737	RT RENAL MASS	T2aNOMO	1.28	RT RAD NEPH	CC RCC GRADE III
14	SHANMUGASUNDHARAM	50/M	29227	RT XGPN		2.64	RT NEPH	XGPN
15	MEHUMUDA	72/F	63441	LT RENAL MASS	T1bNOMO	1.73	LT RAD NEP	PAPILLARY CA GRADE II
16	ALIS BAGYAVATHI	53/F	10822	RT RENAL MASS	T2N1M1	1.18	RT CYT NEPH	CC RCC GRADE IV
17	BANUMATHI	48/F	104911	RT RENAL MASS	T3bN1M0	1.16	RT RAD NEPH	CC RCC GRADE IV
18	ALAMELU	40/F	98976	RT RENAL MASS	T2N0M0	1.39	RT RAD NEPH	CC RCC GRADE II
19	BALADHANDAYUTHAM	51/M	89112	RT RENAL MASS	T1bNOMO	1.68	RT RAD NEPH	CHROMOPHOBE GRADE III
20	PONNUSAMY	49/M	22799	LT RENAL MASS	T3aN0M0	1.4	LT RAD NEP	CC RCC GRADE II
21	RAJAM	59/M	13057	RT METS RCC	T3aN1M1	1.21	RT CYT NEPH	CC RCC GRADE III
22	PANNER	72/M	11476	LT RENAL MASS	T3aN1M1	1.81	LT RAD NEP	PAPILLARY CA GRADE II

23	MOHAN	50/M	29217	RT XGPN		2.84	RT NEPH	XGPN
24	SHANTHI	60/F	56442	RT RENAL MASS	T2bN1M0	1.76	RT RAD NEPH	CHROMOPHOBE GRADE IV
25	SUBRAMANI	65/M	73289	LT RENAL MASS	T3bN1M0	1.28	LT RAD NEPH	CC RCC GRADE III
26	KALA	35/F	12865	LT AML		1.84	LT NEPH	AML
27	HARIDOSS	50/M	19171	RT RENAL MASS	T3bN1M0	1.26	RT RAD NEPH	CC RCC GRADE III
28	PANCHALAI	60/F	13262	AML LT		1.96	LT NEPH	AML
29	KASTHURI	35/F	81532	LT XGPN		2.76	LT NEPH	XGPN
30	POOVARASAN	48/M	20117	RT RENAL MASS	T3aN0M1	1.12	RT CYT NEPH	CC RCC GRADE IV
31	MUNIYAMMAL	48/F	59253	AMLRT		1.68	RT NEPH	AML
32	VATCHALA	54/F	51842	LT RENAL MASS	T2bN1M0	1.44	LT RAD NEPH	CC RCC GRADE II
33	VASANTHI	43/F	21238	BOS III CYST		2.5	RT NEPH	SIMPLE CYST
34	ANNAKILI	59/F	45001	RT RENAL MASS	T3aN0M0	1.63	RT RAD NEPH	COLL DUCT RCC III
35	DILLI BABU	60/M	24735	RT RENAL MASS	T3aN0M0	1.74	RT RAD NEPH	PAPILLARY CA GRADE IV
36	RAJAM	51/M	14254	RT METS RCC	T3aN1M1	1.22	RT CYT NEPH	CC RCC GRADE III
37	SALAMMOL	46/F	86848	LT RENAL MASS	T3aN1M1	1.62	LT RAD NEPH	PAPILLARY CA GRADE IV
38	SUBBURAMAN	65/M	73289	LT METS RCC	T3aN0M1	1.24	LT CYT NEPH	CCRCC GRADE III
39	RAHAMA ULLAH	52/M	51751	RT RENAL MASS	T1bN1M1	1.28	RT RAD NEPH	CC RCC GRADE III
40	ANIKI REDDY	65/M	51732	RT RENAL MASS	T3aN1M1	1.62	LT CYT NEPH	CHROMOPHOB GRADE IV

<u>ஆராய்ச்சி ஒப்புதல் படிவம்</u>

ஆராய்ச்சி தலைப்பு

"பரவல் கனத்த காந்த ஒத்ததிர்வு படமாக்கல் மூலம்
சிறுநீரக கட்டிகளை அறிவதற்கான ஆய்வு"

ஆராய்ச்சி நிலையம் : சிறுநீரியல் துறை,
சென்னை மருத்துவக் கல்லூரி மற்றும்
ராஜீவ் காந்தி அரசு பொது மருத்துவமனை, சென்னை.

பங்கு பெறுவரின் பெயர் :

பாலினம் :

பங்குபெறபவரின் எண் :

பங்கு பெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக்கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கின்றேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிகிறேன். எனது உடல் நலம்பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கதிற்கு மாறான நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்து அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

இந்த ஆய்வில் எனக்கு இரத்தம், சிறுநீர், எக்ஸ்ரே, ஸ்கேன் மற்றும் தசை பரிசோதனை செய்துகொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் ..... இடம்..... தேதி.....

கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம்..... தேதி.....

ஆய்வாளரின் பெயர் .....

தகவல் படிவம்

உபயத்தார்	:	இல்லை
ஆய்வாளர் பெயர்	:	
பங்கேற்பாளர் பெயர்	:	
ஆய்வு செய்யப்படும் தலைப்பு	:	பரவல் கனத்த காந்த ஒத்ததிர்வு படமாக்கல் மூலம் சிறுநீரக கட்டிகளை அறிவதற்கான ஆய்வு

1. இந்த ஆய்வு

தங்களுக்கு சிறுநீகரத்தில் கட்டி ஏற்பட்டு உள்ளது. அதற்கு சிகிச்சை அளிக்கும் முன் உங்களின் நோய்க்குறிய கட்டத்தை அறிய வேண்டி உள்ளது. அதன்பொருட்டு தாங்கள் பரவல் கனத்த காந்த ஒத்ததிர்வு படமாக்கல் மூலம் பரிசோதனை செய்து நோய்குறி கட்டத்தை அறியலாம். எனவே அதற்காக பரவல் கனத்த காந்த ஒத்ததிர்வு படமாக்கல் ஆய்விற்கு சம்மதம் தருமாறு தெரிவித்துக் கொள்கிறேன்.

இந்த ஆய்வில் பங்குபெறுவது நோயாளிகளின் சொந்த விருப்பத்திலேயே ஆகும். இந்த ஆய்வையொட்டி எந்தவிதமான சந்தேகங்களுக்கும் விளக்கம் பெற நோயாளிகளுக்கு உரிமை உள்ளது. இந்த ஆய்வின் முடிவுகள் இறுதியில் பிரசுரிக்கப்படும்.

பங்கேற்பவரின் கையொப்பம் ..... இடம்..... தேதி.....

கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம்..... தேதி.....

ஆய்வாளரின் பெயர் .....

INSTITUTIONAL ETHICS COMMITTEE

MADRAS MEDICAL COLLEGE,CHENNAI -3

Telephone No: 044 25305301

Fax : 044 25363970

CERTIFICATE OF APPROVAL

To,

Dr.D.Mohankumar
II Year M.Ch Urology,
MMC,Chennai -3

Dear D.MOHANKUMAR,

The Institutional Ethics committee of Madras Medical College,reviewed and discussed your application for approval of the proposal entitled "Diffusion weighted MRI in renal masses" No 10062013.

The following members of ethics committee were present in the meeting held on 11.06.2013 conducted at Madras Medical College,Chennai- 3

1. Dr.Sivakumar MS FICS FAIS - Chairperson
2. Prof.R.Nandhini MD - Member secretary
   Director ,Institute of Pharmacology,MMC,Chennai -3

3.Prof.Shyamaraj MD - Member
Director,i/c,Instt.of Biochemistry,MMC,CH-3
4.Prof.P.Karkuzhali MD - Member
Prof.,Instt.of Pathology,MMC,CH-3
5.Prof.A.Radhakrishnan MD - Member
Prof of Internal Medicine
6.Prof.S.Deivanayagam MS - Member
Prof.of surgery,MMC,CH-3
7.Thiru.S.Govindasamy BABL ---------- - lawyer
8.Tmt.Arnold Saulina MA MSW -Social scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman and other members

The institutional ethics committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report.

19/6/13

Member secretary, ethics committee

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003.

20/6/13

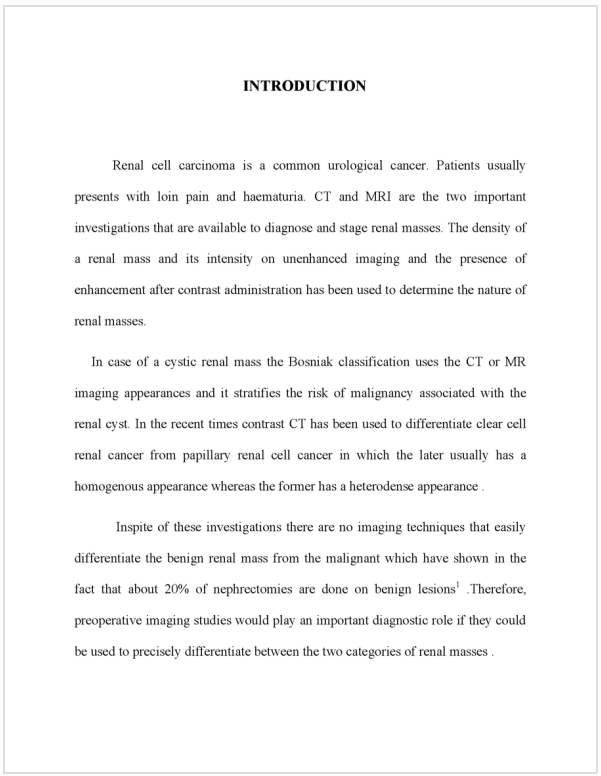
diffusion weighted MRI in renal masses

ORIGINALITY REPORT

20%	4%	18%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Margulis, Vitaly, Surena F. Matin, and Christopher G. Wood. "Benign Renal Tumors", Campbell-Walsh Urology, 2012. Publication	2%
2	Taouli, B., R. K. Thakur, L. Mannelli, J. S. Babb, S. Kim, E. M. Hecht, V. S. Lee, and G. M. Israel. "Renal Lesions: Characterization with Diffusion-weighted Imaging versus Contrast-enhanced MR Imaging1", Radiology, 2009. Publication	2%
3	Campbell, Steven C., and Brian R. Lane. "Malignant Renal Tumors", Campbell-Walsh Urology, 2012. Publication	2%
4	Nagaraj-Setty Holalkere. "Renal Cell Carcinoma", Medical Radiology, 2010 Publication	1%
5	Submitted to October University for Modern Sciences and Arts (MSA) Student Paper	1%



INTRODUCTION

Renal cell carcinoma is a common urological cancer. Patients usually presents with loin pain and haematuria. CT and MRI are the two important investigations that are available to diagnose and stage renal masses. The density of a renal mass and its intensity on unenhanced imaging and the presence of enhancement after contrast administration has been used to determine the nature of renal masses.

In case of a cystic renal mass the Bosniak classification uses the CT or MR imaging appearances and it stratifies the risk of malignancy associated with the renal cyst. In the recent times contrast CT has been used to differentiate clear cell renal cancer from papillary renal cell cancer in which the later usually has a homogenous appearance whereas the former has a heterodense appearance .

Inspite of these investigations there are no imaging techniques that easily differentiate the benign renal mass from the malignant which have shown in the fact that about 20% of nephrectomies are done on benign lesions[1] .Therefore, preoperative imaging studies would play an important diagnostic role if they could be used to precisely differentiate between the two categories of renal masses .